

logists have emphasised that it may arise either in patients with active leprosy or, more commonly, in those who have had leprosy (Muir 1948, Browne 1965). Schulz (1965) found normal vitamin-A levels in the blood of leprosy patients with ichthyosiform changes in the skin.

In our patients hydration alone relieved the condition, but dry skin reappeared when daily hydration was discontinued. This suggests strongly that the important factor is the water content of the skin, and that loss of water from the surface of the skin should be prevented, after hydration, by means of a hydrophobic barrier. This suggestion is supported by the observation that dry skin occurs in those situations where there is an irreversible deficiency of endogenous hydration.

Blank (1952) found that human skin becomes brittle when its water content falls below 10 mg. per 100 mg. dry skin. It seems that as long as the relative humidity of the atmosphere is 60% or over, an equilibrium exists between air and skin, and excessive skin drying does not take place. Gaul and Underwood (1952) also found a direct association between air moisture and smoothness and suppleness of the skin. In the patients described by us the dryness of the tropical atmosphere was an important contributory factor in the occurrence of dry skin, in addition to the cutaneous anaesthesia and diminished sweating already referred to.

In leprosy patients, other advantages follow hydration of the skin besides the prevention of fissuring with its risk of deep inflammation. The softening of localised hard callus at the sites of pressure on the soles of the feet reduces the liability to plantar ulceration. Skin texture, also, is improved noticeably, and this enhances the degree of tactile and thermal appreciation remaining. Hydration of the skin reduces the risk of burning. Leprosy patients frequently burn themselves by holding utensils that are too hot for the normal person to touch. The patient with gross impairment of peripheral sensation discovers—as does the Indian fire-walker who immerses his feet in water for hours before performing—that hydrated skin is a less efficient conductor of heat than hard, horny skin.

Although this report mainly concerns leprosy patients, the findings presented seem to be applicable to the dry skin of other conditions, to judge from our investigations made in Africa and India on patients who do not have leprosy.

Summary

Dry skin is a frequent and serious complication of leprosy. The low water content of the skin is associated with diminished sweating and peripheral neuropathy, and aggravated by low atmospheric humidity. Dry skin in leprosy, and probably in other conditions, may be relieved, and fissuring prevented, by daily soaking of the affected part in water, followed by an application of soft paraffin.

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JOB'S SYNDROME

Recurrent, "Cold", Staphylococcal Abscesses

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"So went Satan forth from the presence of the Lord, and smote Job with sore boils from the sole of his foot unto his crown".—*Job*, II, 7.

WE have examined two girls who have had recurrent, "cold", staphylococcal abscesses since birth. The staphylococci do not seem to be unusually virulent, and neither child has diabetes or any other condition known to predispose to infection. Since we are not aware that any similar cases have been described previously, we report these cases in detail.

Case-reports

FIRST CASE

The patient is a nine-year-old girl who was originally referred, aged seven, to the University of Washington Hospital. She was normal at birth but at three weeks she had eczema which became infected. She later had recurrent ear, nose, and sinus infections which were treated many times with antibiotics. At three years a tonsillectomy was done because of chronic otitis media. During the next few months she had furuncles of the buttocks, abdomen, and extremities. At forty-five months she had severe left-cervical adenitis which was treated with antibiotics and incision and drainage. Culture of pus from the cervical abscess grew staphylococci which were resistant to penicillin, tetracycline, erythromycin, and streptomycin (P., T., E., and S.). Three weeks later she had right-lower-lobe pneumonia which responded to treatment with oxacillin. At forty-seven months she had furuncles on the face and cellulitis about the right eye. She was referred for evaluation because of the persistent skin, ear, sinus, and mastoid infections.

On clinical examination she was noted to have red hair, fair skin, seborrhoea of the scalp, many scars from old abscesses, atrophic skin over the cheeks, weeping lesions about both ears, perforated tympanic membranes, chronic conjunctivitis, drainage and crusting about the nose, dental caries, and atrophic changes about the fingernails. Her height and weight were at the 10th percentile for age (Nelson 1964). There was no lymphadenopathy or hepatosplenomegaly.

Hæmatocrit, white-blood-cell count, platelets, and urinalysis were normal. The sweat chloride was 6.8 mEq. per litre. Examination of the bone marrow showed normal cellular elements and decreased iron stores. Intermediate strength purified protein derivative of tuberculin and fungus skin-tests were negative. A battery of scratch tests for allergies was negative. X-rays showed maxillary and ethmoid sinusitis, bilateral mastoiditis, and a persistent infiltrate in the lower lobe of the right lung. Tests of immunological function are summarised in the accompanying table.

She was started on intermittent oxacillin, prophylactically. Infections continued to recur, and continuous therapy was started with 500 mg. of oxacillin three times a day.

At age seven years and four months, while on oxacillin prophylaxis, she had a 6 cm. × 10 cm. mass in the anterior midline of the neck which extended along the left mandible. There was no fever or cervical lymphadenopathy. The mass was only slightly tender and did not feel warmer than the rest of the body. The hospital surgeons thought that the mass was an enlarged, thyroglossal-duct cyst which was not infected. The white-blood-cell count was 12,000 per c.mm. with 66% neutrophils, 25% lymphocytes, 5% monocytes, and 4%

IMMUNOLOGICAL STUDIES

Test	Case 1	Case 2
Serum-protein immunoelectrophoresis	Normal immunoglobulin pattern	Normal immunoglobulin pattern
Blood-type	A	O
Isohæmoagglutinin titre	Anti-B (1/128)	Anti-A (1/16) Anti-B (1/4)
Schick	Negative	Negative
Typhoid-H titre	>1/160 (3 immunisations)	1/320 (4 immunisations)
Staphylococcal agglutinin titre* (normal 1/40 to 1/640)	1/320	1/640
Bone-marrow plasma-cells	Normal	Normal
Inflammatory cycle†	Normal	Normal
Phagocytosis in vitro‡	Normal	Normal

* By the method of Boger et al. (1960).
† By the method of Rebusck and Crowley (1955).
‡ By the method of Ecker and Lopez-Castro (1947) with *Staph. aureus* as the object of phagocytosis.

eosinophils. The mass was incised and 200 ml. of purulent material was obtained. Culture of the pus grew staphylococci resistant to P., T., E., and S. Pus drained intermittently and, two months later, a necrotic lymph-node was excised from the neck. Culture of this abscess also grew out staphylococci resistant to P., T., E., and S. Three weeks later she had another mass in the neck which was only slightly tender and erythematous. The mass was incised and a culture grew staphylococci resistant to P., T., E., and S. Seven days of intensive therapy with intramuscular oxacillin resulted in decreased drainage from the neck lesion and partial clearing of infected skin lesions about the eyes and ears.

The neck lesion drained occasionally over the next year and twice required incision. Staphylococci, resistant to P., T., E., and S., were cultured both times. At eight years and five months, she had a tooth abscess: the tooth extracted. Culture of this abscess grew out β -hæmolytic streptococci which were not group A, B, C, D, or G. Three months later the old abscess site in the neck again drained, and the cultures grew staphylococci resistant to P., T., E., and S.

Through the time of observation at this hospital, the patient has had intermittent drainage from both ears, recurrent skin infections about the nose, eyes, and ears, and occasional furuncles on the face, arms, and extremities. Many cultures for mycobacteria have been negative. The only organisms isolated from closed lesions in this patient have been coagulase-positive *Staphylococcus aureus*, resistant to P., T., E., and S. Similar staphylococci have frequently been cultured from open lesions, although other organisms have also been found occasionally. She is at present much improved, and is receiving oxacillin, 2000 mg. daily, and frequent hexachlorophene baths.

Both parents, an older half-brother, and two younger sisters have been well. None has had staphylococcal infections.

SECOND CASE

The patient is a six-year-old girl who was referred to this hospital, aged two. Her birth weight after a normal-term pregnancy was 2300 g. (5 lb.). The only abnormality noted at birth was hyperextensible joints. At two weeks, eczema appeared on the face and spread to involve the neck and flexor surfaces of the extremities. At four months the eczema became worse, and she was treated for five days in a hospital. The rash improved but then became worse, and she was admitted to the hospital for a second time at five months. During that hospitalisation, she had an abscess over the medial aspect of her right knee which required incision and drainage. She then began having frequent subcutaneous abscesses of the scalp, neck, back, buttocks, and knees. Several observers noted independently that the abscesses had remarkably little local erythema or tenderness. Cultures of these abscesses have always grown *Staph. aureus*. Many cultures for

mycobacteria and fungi have been negative. She continued to have weeping, crusting lesions about the ears, eyelids, and nose. She also had a chronic, purulent, nasal discharge and many infected skin lesions over the flexor surfaces of the arms and legs.

When first seen at this hospital, she was a small, active child with fair skin and bright-red hair. Her height and weight were well below the 3rd percentile for age (Nelson 1964). There were numerous scars from the abscesses that had been drained. On the buttocks were two large non-tender abscesses which were 6 cm. in diameter. There was another large, non-tender abscess on the back of the neck. Weeping, crusting lesions were present about the ears, eyes, and nose. Joints of the extremities were hyperextensible. There was no lymphadenopathy or hepatosplenomegaly.

Hæmatocrit and urinalysis were normal. The white-blood-cell count was 18,000 per c.mm. with 64% neutrophils, 33% lymphocytes, and 3% monocytes. Platelets were normal. The bone marrow was hypercellular with a normal myeloid-erythroid ratio and a notable eosinophilia. The sweat chloride was 16 mEq. per litre. Intermediate strength PPD and fungus skin-tests were negative. A battery of scratch tests for allergies was negative. X-rays of the skull showed premature closure of the sagittal suture. X-rays of the chest and long bones were normal.

She improved somewhat with occasional antibiotic therapy and hexachlorophene baths, though she still required occasional incisions for drainage of abscesses. At three years she had cough, fever, and large abscesses of the right buttock and left thigh. She was admitted to hospital and was found to have multiple, staphylococcal abscesses, staphylococcal pneumonia, cardiomegaly, and congestive heart-failure. Staphylococci isolated from the abscesses were resistant to penicillin. She was critically ill for two weeks but responded to therapy with methicillin, digitalis, diuretics, and large doses of gamma-globulin.

She improved for the next three months but then infections recurred about the eyes and ears and she had an abscess on the forehead. The abscess was noted to have little warmth, tenderness, or redness. Cultures of the pus from this abscess grew staphylococci, resistant to penicillin. She was started on intermittent cloxacillin therapy, 500 mg. for four days a week. During the next five months she had an abscess of the right thigh and an abscess on the neck.

At four years she began having a persistent cough. Staphylococci and normal flora were isolated from sputum cultures. Chest X-ray showed bilateral bronchiectasis, and postural drainage was begun three times daily.

Over the next year and a half she was relatively asymptomatic and free of severe infection. She continued to have periodic recurrences of infections about the eyes, cheek, and ears. Occasionally, pus drained from both ears, and infected eczematoid lesions appeared on the elbows and knees. She also continued to have a mild, chronic cough. Mild clubbing of the fingers was noted at the age of five and a half.

At age five years and nine months her height was 94 cm. and her weight was 10.5 kg. (23 lb.). She had no new symptoms and was attending school regularly. Chest X-ray showed new extensive, bilateral, pulmonary infiltrates in the right middle lobe and the lingula of the left upper lobe. The infiltrates did not clear with increased postural drainage and antibiotic therapy and, one month later, she was started on a home-care programme of mist and aerosol therapy for her pulmonary disease. She improved remarkably within a week. Her appetite increased greatly and the pulmonary infiltrates partly cleared.

The only organisms isolated from closed lesions in this patient were coagulase positive *Staph. aureus*, resistant to penicillin. Cultures of open infections grew similar staphylococci, although other bacteria were isolated occasionally.

Both parents and three siblings are well. None has had staphylococcal abscesses, skin infections, or eczema. A sister and a brother are of normal height and weight. The other sister physically resembles the patient, having hyperextensible

joints and very small stature, but has not had frequent infections.

Discussion

The common features of these two patients include fair skin, red hair, and recurrent, "cold", staphylococcal abscesses. Both have chronic, purulent, nasal discharge, sinusitis, chronic otitis media, and infected eczematoid skin lesions. Both have pulmonary disease, although this has been more severe in the case 2 than in case 1. The antibiotic-sensitivity pattern of the staphylococci isolated from each patient has not changed over several years, and all the infections in each patient may have been caused by the same strain. It seems unlikely, however, that the infections have been caused by unusually virulent staphylococci, because the parents and siblings have not had staphylococcal infections.

The manifestations of these patients are clearly distinct from the immunological-deficiency syndromes, which include agammaglobulinæmia, Chediak-Higashi syndrome, Aldrich syndrome, and ataxia-telangiectasia (Good et al. 1962). There was no evidence of systemic diseases such as leukæmia, lymphoma, or reticulo-endotheliosis. The clinical signs were similar to those of the syndrome of progressive septic granulomatosis reported by Carson et al. (1965). Patients with this syndrome have pigmented, lipid histiocytes, chronic lymphadenitis, chronic dermatitis, chronic pulmonary disease, and fatal infections. In contrast with the cases presented here, patients with progressive septic granulomatosis have been males with hepatosplenomegaly who were infected with bacteria other than staphylococci; they have not been reported as having "cold" abscesses.

We suggest that these patients have a defect which makes them unusually susceptible to staphylococci. Since the mechanisms of resistance to staphylococcal infections are not understood, it is difficult to suggest a specific defect. No abnormality was found in serum-immunoglobulins, antibody formation, inflammatory cycle, or phagocytosis in vitro. Two observations on these patients may be relevant. The first is that despite years of recurrent abscesses, there were few systemic infections. Therefore, the patients probably have normal "systemic" resistance to staphylococcal infections. The second observation is that the abscesses are cold. Miles (1956) has shown that the first few minutes after bacteria have been injected into the skin constitutes the decisive period for inflammation. Local nonspecific factors are probably of primary importance during the decisive period. We suggest that these patients have a defect in local nonspecific mechanisms of resistance. Perhaps there is an abnormality of the mediators of the acute inflammatory response (Spector 1964).

The pitiful appearance of these patients and the history of recurrent abscesses and skin infections makes the name "Job's syndrome" seem suitable.

Summary

Two girls with life-long histories of "cold" staphylococcal abscesses are described. The signs were different from those of the recognised syndromes of recurrent infections. The infections were partially controlled with continuous antibiotic prophylaxis. It is suggested that the patients have a defect in local resistance to staphylococcal infections.

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Preliminary Communication

LOSS OF EJACULATION IN MALE RHESUS MONKEYS AFTER ADMINISTRATION OF PROGESTERONE TO THEIR FEMALE PARTNERS

THE endocrine factors concerned in the control of primate sexual behaviour are imperfectly understood but, although little studied, have special relevance for the human situation. Observations in the field have shown that, at the time of greatest sexual skin swelling in the baboon, which is usually near mid-cycle, the males show most interest in the females.^{1 2} In the laboratory, rhythmic changes in sexual behaviour have been noted to be related to the menstrual cycle of the female.³⁻⁵ We have found that, in ovariectomised rhesus monkeys given hormone-replacement treatments, the sexual interactions between opposite-sexed pairs are strikingly influenced by the administration of œstradiol and progesterone.^{6 7} The most notable finding is that dramatic changes in the sexual behaviour of males result when hormones are administered to their female partners: œstradiol stimulates male copulatory activity and progesterone depresses it. We describe here some further work on the depression of sexual activity in the male after the administration of progesterone to the female.

METHODS

Three adult, sexually active male and three mature, female rhesus monkeys were investigated for a period of 18 months. Two females were paired with each male, making a total of six paired combinations. The females were regularly introduced, by means of a transfer cage, into the home cages of the males for testing sessions of 60 minutes. Between tests, animals were housed in individual cages without access to each other. Experienced observers recorded the behaviour during testing sessions from behind a one-way vision mirror, and components of the behaviour observed were quantified by means of a scoring system in terms of time, sequence, and frequency. After bilateral ovariectomy, the females were allowed 10, 16, and 41 weeks respectively to attain a basal condition, at which time routine testing was commenced. After a further 4 weeks, œstrogen was administered to the females in two different

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